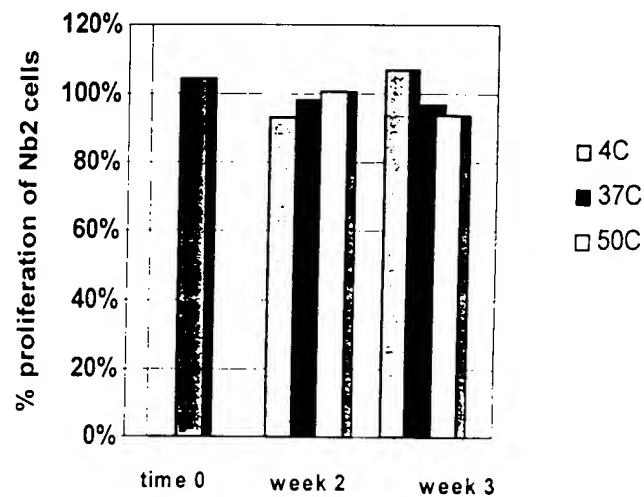


**Figure 1**



**Figure 2**

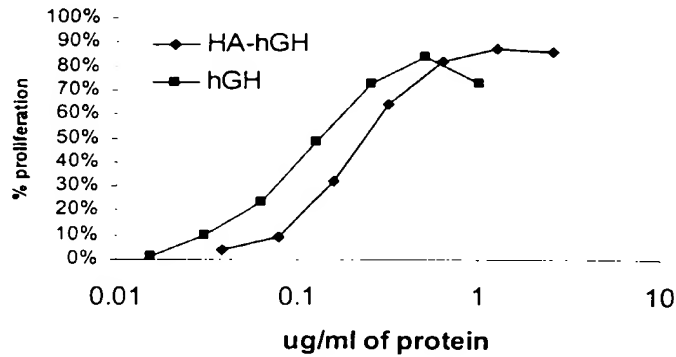


Figure 3A

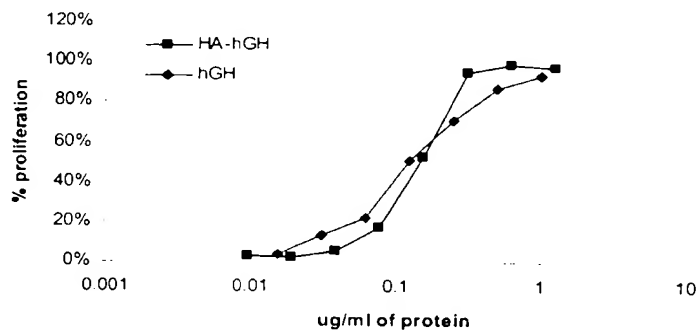
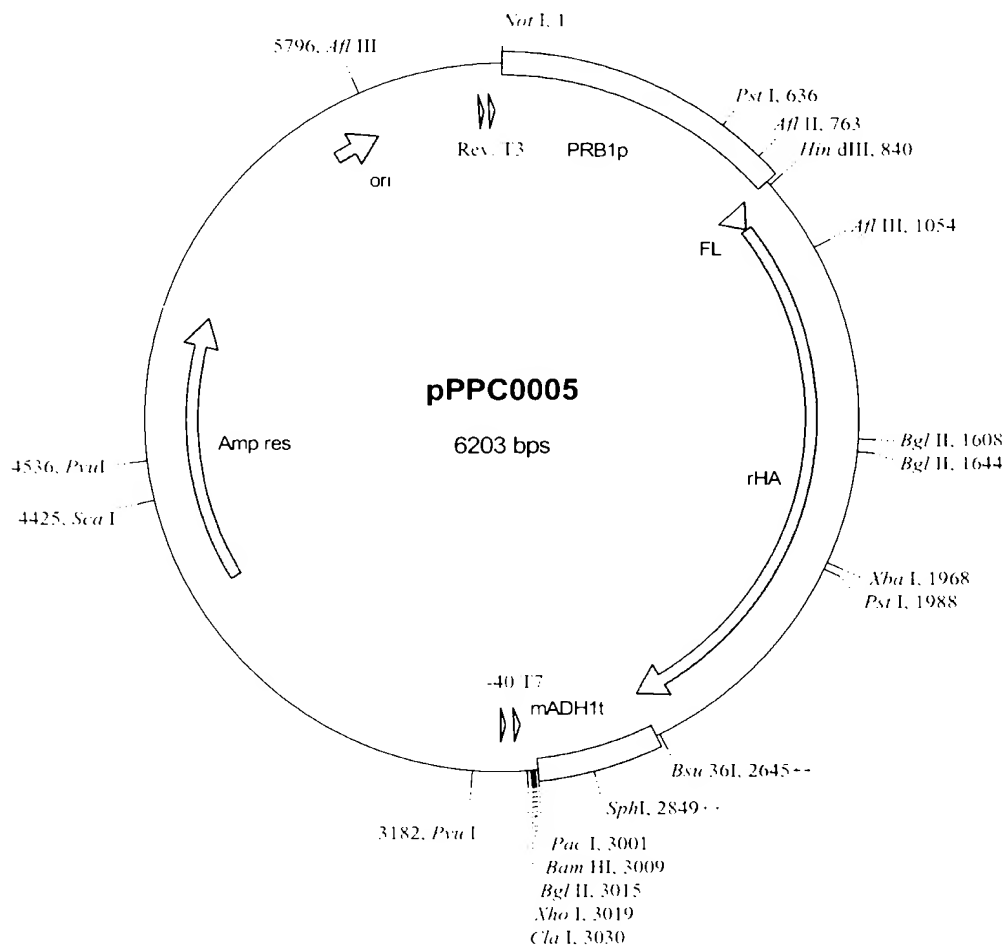


Figure 3B



**Figure 4**

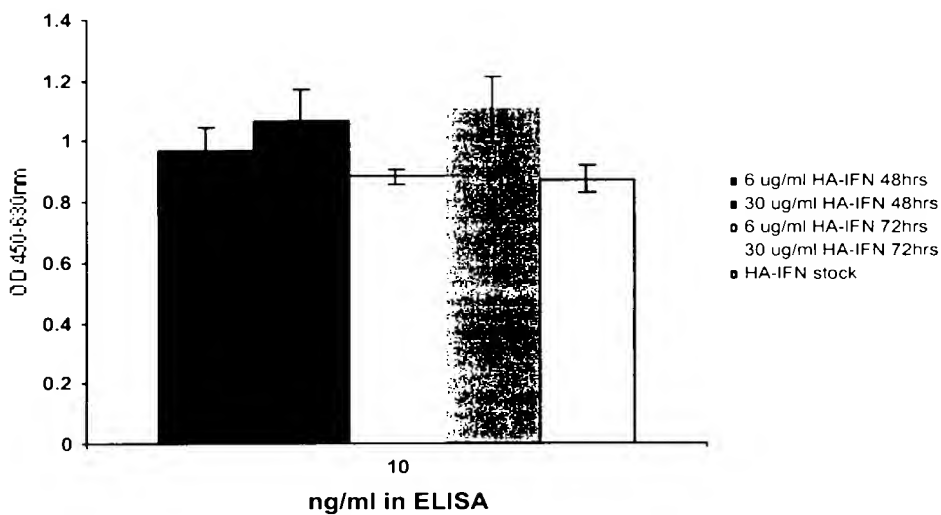


Figure 6

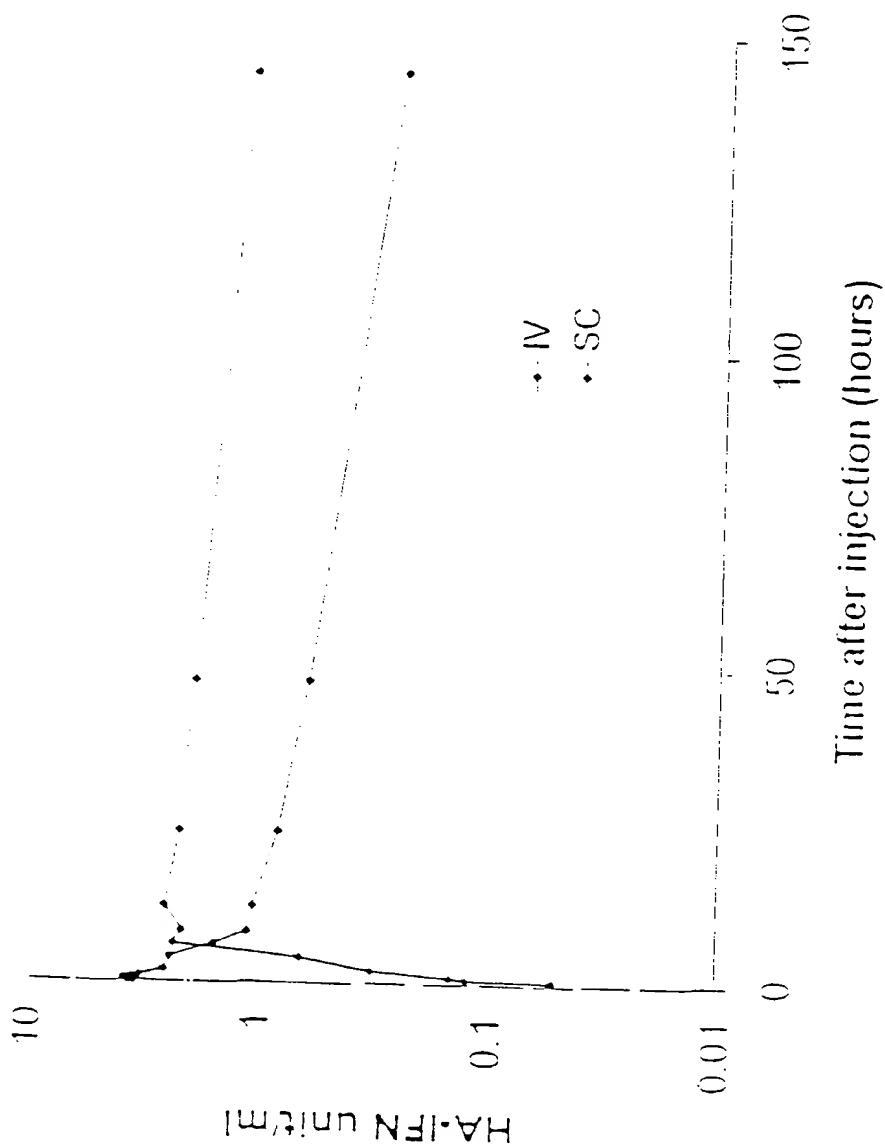
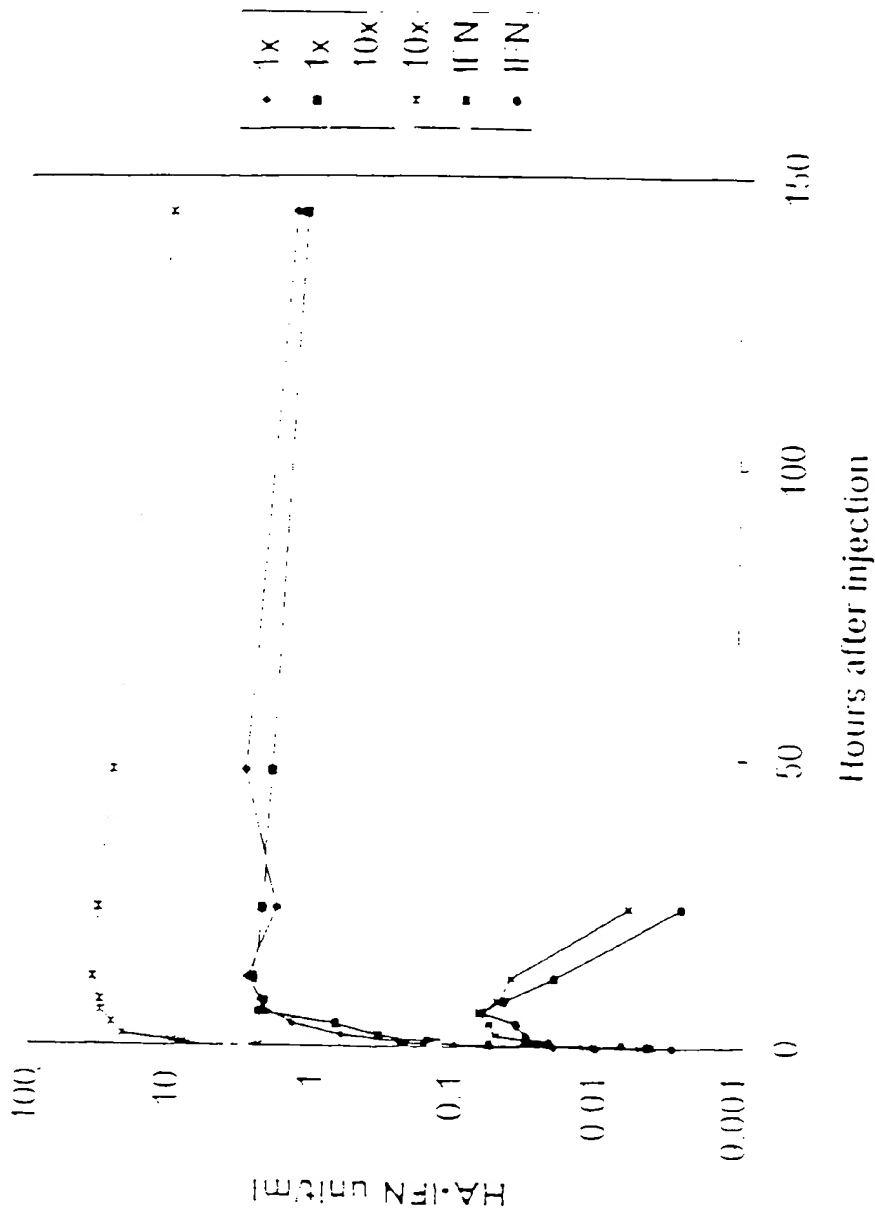


Figure 7



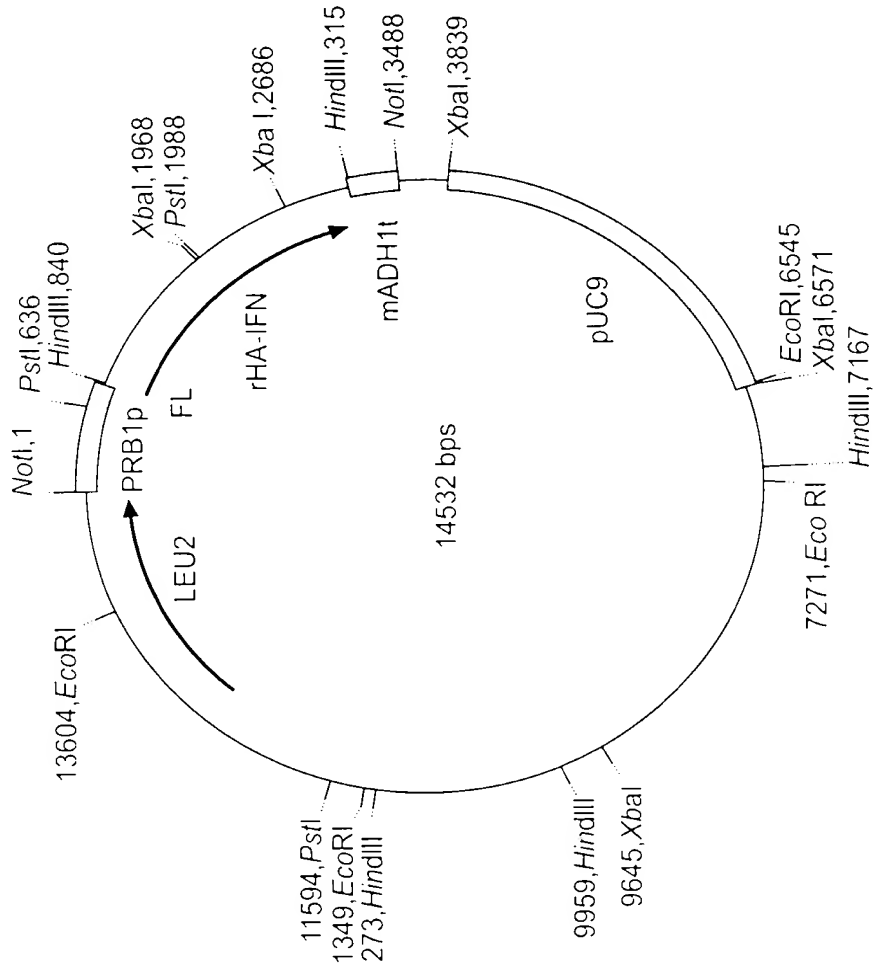


FIG. 8



## Figure 9

```

1   DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQQCPFEDHV KLVNEVTEFA
    HHHHH HHH HHH HHHHHHHHHH HHHHH HHHHHHHHHH

      I                      II                      III
51  KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMACD CAKOEPERNE
    HHHHH HHHHH HHHHH HHHH H HHHH

101 CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY
    HHHH H HHHHHHHH HHHHHHHHH HHHHH

      IV
151 APELLFFAKR YKAAFTECCO AADKAACLLP KLDELRLDEGK ASSAKQRLKC
    HHHHHHHHHH HHHHHHHHH HHHHH HHHHHHHHHH HHHHHHHHHH

      V
201 ASLQKFGEPA FKAWAVARLS QRFPKAEFAE VSKLVTDLTK VHTECCHGDL
    HHHHH HH HHHHHHHHHH HH HHH HHHHHHHHHH HHHHHH HH

      VI                      VII
251 LECADDPADL AKYICENODS ISSKLKECCE KPLLEKSHCI AEVENDEMPA
    HHHHHHHHHH HHHHH HHHHH HHHHHH H

301 DLPSLAADPV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLRLA
    HHHH HHHHH HHHHHH HHHHH HHHHHHHH

      VIII
351 KTYETTLKCK CAAADPHECY AKVFDEFKPL VEEPQNLIKQ NCLEFEQLGE
    HHHHHHHHHH HH H HHHHH HHHHHHHHHH HHHHHH

      IX
401 YKFNALLVR YTKKVPQVST FTLVNSRNIL GKVGSKCKKH PEAKRMPCAE
    HHHHHHHHHH HHHH H HHHHHHHHHH HHH HHHHHHHH

      X                      XI
451 DYLSVVLNQL CVLHEKTPVS DRVTKCTES LVNRRPPCFSA LEVDETYVPK
    HHHHHHHHHH HHHHH HHHHHHHHHH HHHHHHHH

501 EFNATFTFH ADICTLSEKE RCIKKITALY ELVHKPKAT KEQLKAVMDD
    HHH HHH HHHHHHHHHH HHH HHHHHHHH

      XII
551 FFAFVEKCKK ADDKETCPAE ECKKLVAASL AALGL
    HHHHHHHH HHHH HHHHHHHHHH HH
  
```

### Loop

```

I   Val154-Asn61
II  Thr76-Asp89
III Ala90-Glu100
IV  Gln170-Ala176
V   His247-Glu252
VI  Glu246-Glu277
  
```

### Loop

```

VII  Glu280-His288
VIII Ala262-Glu368
IX   Lys439-Pro447
X    Val460-Lys475
XI   Thr478-Pro486
XII  Lys460-Thr466
  
```

## Figure 10

### a. Randomisation of Loop IV.

IV  
 151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC  
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

IV  
 151 APELLFFAKR YKAAFTECCX XXXXXXCLLP KLDEL RDEGK ASSAKQRLKC  
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

X represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

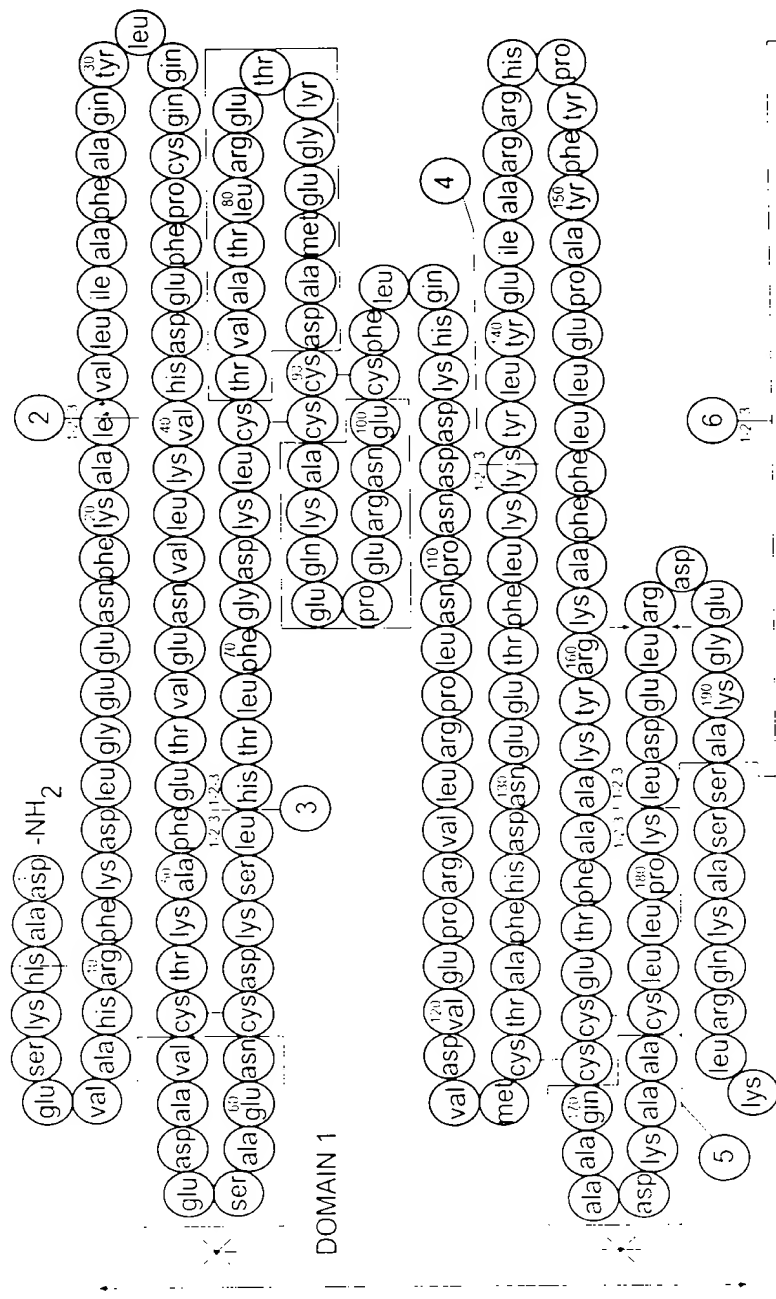
### b. Insertion (or replacement) of Randomised sequence into Loop IV.

(X)<sub>n</sub>



IV  
 151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC  
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 8, 12, 20 or 25.

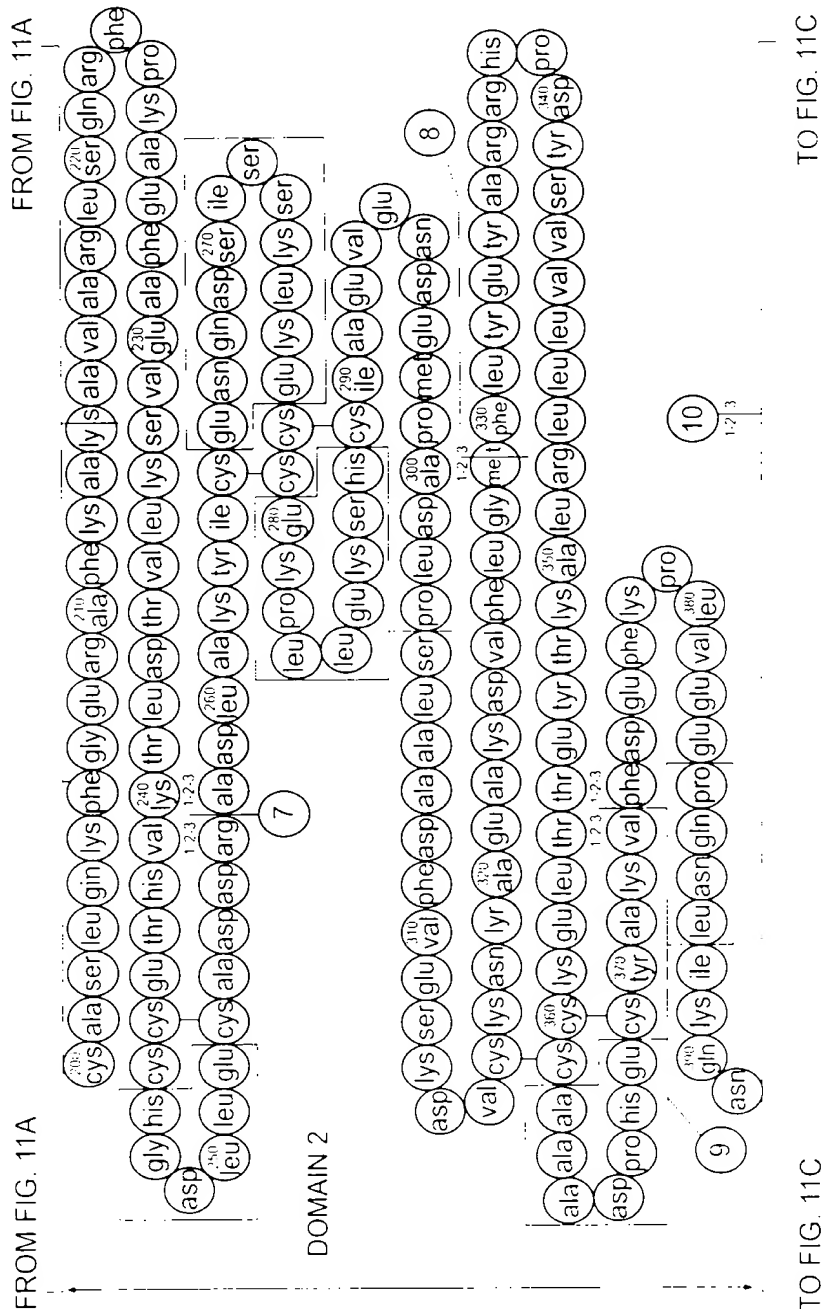


DOMAIN 1

TO FIG. 11B

TO FIG. 11B

**FIG. 11A**



**FIG. 11B**

FROM FIG. 11B

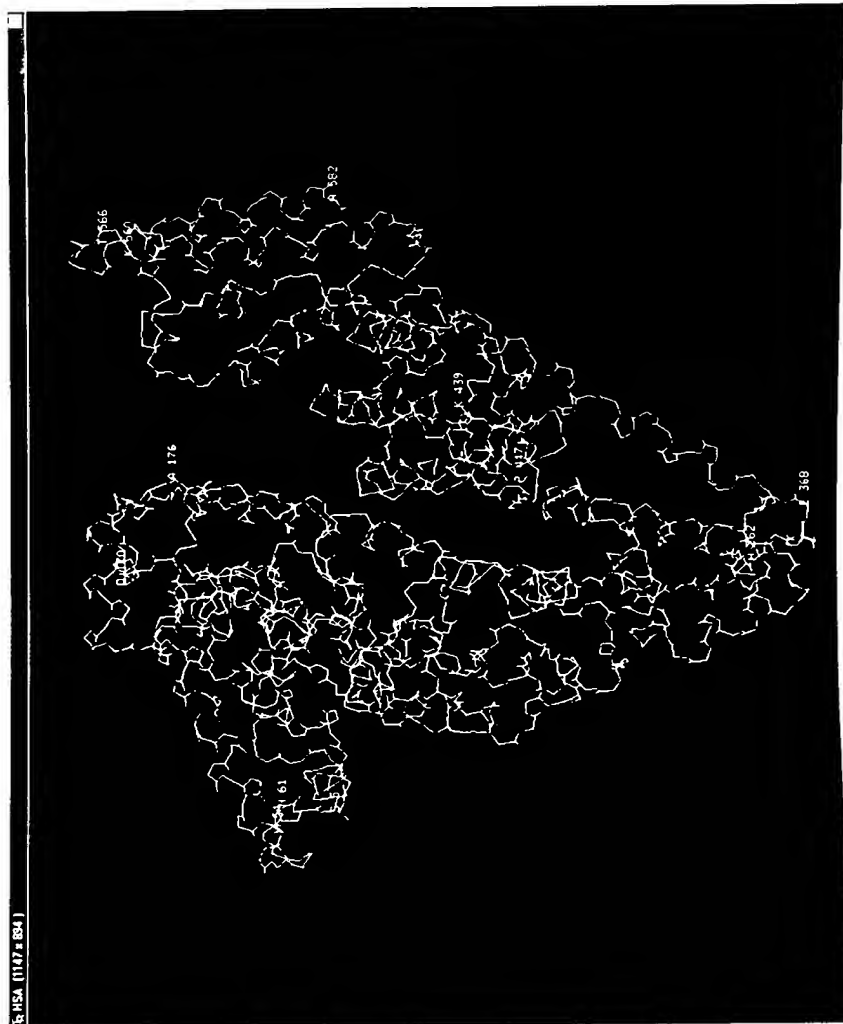


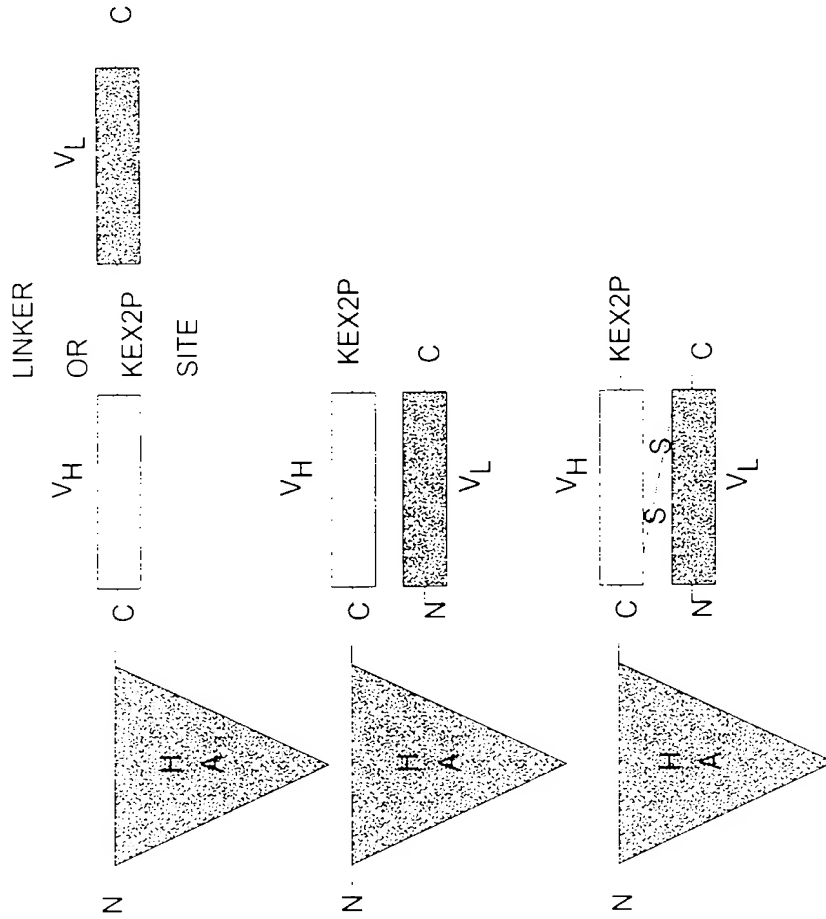
**FIG. 11C**



DISULFIDE BONDS SHOWN IN YELLOW

**FIG. 12:**  
LOOP IV GLU170-A176





**FIG. 14**



1	GAT	GAA	CAG	AAG	AGT	GAG	GTT	GCT	CAT	CGG	TTT	AAA	GAT	TTG	GGA	GAA	AAU	TTC	AAA	60
10	A	B	K	S	E	V	A	H	R	F	K	D	G	G	E	E	N	F	K	70
21	TTG	CTG	CTG	ATT	ATG	TTT	GCT	CGG	TAT	CTT	CGG	CAG	TGT	GCA	TTT	GAA	GAT	CAT	GTA	120
31	A	G	L	I	A	F	A	Q	I	L	Q	Q	I	P	F	E	D	H	V	40
41	AAA	TGA	CTG	AAT	GGA	GGA	ACT	GGA	TTT	CGA	AAA	AGA	TGT	TTT	GCT	GAT	GAG	TCA	GCT	180
51	F	G	L	E	V	T	E	F	A	K	T	C	Y	A	D	E	S	A	E	60
61	AAU	UAT	AG	AAA	UUA	TTT	CAT	AGT	CTT	TTG	GGA	GAG	AAA	TGA	TGG	ACA	GTT	GCA	ACT	240
71	C	D	E	S	I	H	T	L	F	G	D	K	L	C	T	V	A	T	L	80
81	GCT	GAA	ATT	TAT	GCT	GAA	ATT	AGT	TTT	GAG	TTT	TGT	GGA	AAA	GAA	GAA	GCT	GAG	ACA	300
91	P	E	T	Y	G	E	H	A	D	I	A	K	Q	E	F	E	R	N	E	100
101	TTG	CTG	CTG	CTG	AAA	GAT	GAT	GAG	AAA	AAA	CTG	CCC	GGA	TTG	CTG	AGA	CCA	GAG	GTT	360
111	F	L	Q	E	H	D	D	D	H	F	H	L	F	R	L	V	R	P	E	120
121	GAT	CTG	ATG	TGT	ACT	GCT	TTT	CAT	GAT	GAT	AAA	GAG	ACA	TTT	TTG	AAA	AAA	TAC	TTA	420
131	I	C	H	C	T	A	F	H	D	H	E	T	F	L	K	K	Y	L	Y	140
141	GGA	ATT	GAT	AGA	AGA	CAT	CCT	TAC	TTT	TAT	CCC	CCG	GAA	CTC	CTT	TTC	TTT	GCT	AAA	480
151	E	I	A	R	R	H	P	Y	F	Y	A	P	E	L	L	F	F	A	K	160

**Figure 15A**

141 TAT AAA GGT GGT TTT ATA GAA TGT TGG GAA GCT GGT GAT AAA GCT GTC TGC CTG TTG CCA 540  
 161 Y E A A F T E C Q A A D K A A C L L P 180

341 AAG CTT GAT GAA CTT CCG GAT GAA CCG AAG GCT TCG TCT GCG AAA CAG AGA CTC AAA TGT 600  
 141 F I D E L R D E G E A S S A E Q R L K C 200

541 TCG AAT CTT GAA AAA TTT GGA GAA AAA GCT TTC AAA GCA TGG GCA CTG GCT CCG CTG AGC 660  
 141 A S L Q E F G E E K A F K A W A V A R L S 220

741 CAG AAA TTT CCG AAA GCT GAG TTT GCA GAA GCT TCC AAG TTA GTG ACA GAT CTT ACC AAA 720  
 221 Q R F F A E F A E V S K L V T D L T K 240

941 CTC CAC AAG GAA TCG CCG GAT GAT CTG CTT GAA TGT GCT GAT GAC AGG GCG GAC CTT 780  
 341 V H T E C A E E D L L E C A D D R A D L 260

1141 TCG AAG TAT AAT TCG GAA AAA CAG GAT TCG ATC TCG AGT AAA CTG AAG GAA TGC TGT GAA 840  
 141 A E I C E H P D S I S S E L K E C E 280

1341 AAA GCT CCG TTG GAA AAA TCG CAC TGC ATT CCG GAA GTG GAA AAT GAT GAG ATG CCT GCT 900  
 241 K F L L E K S H C I A E V E H D E M P A 300

1541 GAC TTG CTT TCA TTA GCT GCT GAT TTT GTT GAA AGT AAG CAT GTT TGC AAA AAC TAT GCT 960  
 301 D L P S L A A D F V E S K D V C K N Y A 320

Figure 15B

461 AAC GCA AAG GAT GTC TTC GAG GGC AGG TTT TTG TAT GAA TAT GCA AGA AGG CAT CCT GAT 1020  
 471 E A K D V F L G M F L Y E T A R R H P D 340  
  
 1031 TAC TTT GTC CTC GCG GAG GAT TGC AAG ACA TAT GAA AGC ACT GTA GAG AAG TGC 1980  
 1041 E S T V L L L R L A K T Y E T T L E K C 360  
  
 1061 TGT TGC GGT TCA GAG GAT CAT GAA TGC TAT GGC AAA GTC GAT GAA TTT AAA CCT CTT 1140  
 1071 A A A A D I E C Y A K V F D E F K P L 380  
  
 1141 GTG GAA GGC GGT CAG AAA TTA AGC AAA GAA AAC TGT GAG GAT TTT GAG CAG CTT GGA GAG 1200  
 1151 V E E F V S I I K C H C E L F E Q L G E 400  
  
 1171 TAC AAA TTC AAG AAT GTC TCA TTA GTC GTC TTA GTC TGT TAC AGC AAG AAA GTA CCC GAA GTG TCA ACT 1260  
 1181 E F V S E A L E C V P Y T K E Y P Q V S T 420  
  
 1201 TCA AAT GTC GGC GTC TCA AAA AAG TTA TCA AAA GTG GGC AGC AAA TGT TGT AAA CAT 1320  
 1211 I S T V E V E E H L G K V E S K C K H 440  
  
 1231 GGT GAA TCA AAA AAG AAG GTC TAT GCA GAA GAG TAT CTA TGC GTG GTC CTG AAC CAG TTA 1380  
 1241 E A A K E V C A E D Y L S V V L N Q L 460  
  
 1261 TGT GCG TTT TAT GAT AAA AGC GCA GTA ACT GAC AGA GTC ACA AAA TGC TGC ACA GAG TCC 1440  
 1271 C V L H E K T P V S D R V T K C C T E S 480

Figure 15C

1441 TTG GTG AAC AAG GAA GAA TGC TTT TCA GCT CTG GAA GTC GAT GAA ACA TAC GTT GCC AAA 1500  
 481 L V H R R P C F S A L E V D E T Y V P K 500

1501 GAG TTT AAT GCT GAA ACA TGC ACG TTC GAT GAT ATA TGC ACA GTT TCT GAG AAG GAG 1560  
 501 E F H A E T F T F H A D I C T L S E K E 520

1561 AGA GAA AAG AAC AAA GAA AAT TTA GTT GTT GAG GTT CTG AAA GAC AAG GCC AAG GCA ACA 1620  
 521 R Q I K F Q T A G V E L V K H K P K A T 540

1621 AAA GAG GAA CTG AAA GTT GTT AAG GAT GAT TTC GAA GCT TTT GTA GAG AAG TGC TGC AAG 1680  
 541 K E Q L K A V M D D F A A F V E K C C K 560

1681 GCT GAG GAT AAA GAG AAG TAT TTT GAG GAG GAT AAA AAA GTT GTT GCT GCA AGT CAA 1740  
 561 A D D K E T C F A E E G K K L V A A S Q 580

1741 GCT GAG TTA GAG TTA GAA GAT TTA GAT TTA AAA GCA TCT GAG 1782  
 581 A A G G L 585

Figure 15D